



## Precision Medicine in Pharmacy Design: Pharmacogenomics & Pharmacogenetics

Pharmacogenomics, Precision Medicine, Pharmacogenetics, human genome and genetic testing have become frequent terms that benefit leaders and consultants use as they design their benefit offerings, particularly with pharmacy benefits. However, the use of these tools and tests are not new.

In fact, Pharmacogenetics have existed since [510 BC when Pythagoras](#) noted that ingestion of fava beans resulted in a fatal reaction in some, but not all, individuals due to an internal deficiency.

This report will explore how these terms characterize ways an individual's genes affect their response to medications and how they are being used specifically within the pharmacy benefit for self-insured employers. In addition, clinical and administrative guidance is provided, along with action steps employers can take to best utilize Pharmacogenomic (PGx) testing.

As high-cost biologics and other specialty drugs continue to come to market, PGx has the potential to have the greatest impact on precision medicine within pharmacy benefit design.

The role of PGx testing has a significant place in determining which drugs match best to which patients in the right amounts at the right time. Absent a good pharmacy benefit strategy that employs PGx testing effectively within specialty drug design, biologic drug use can be more costly and prescribed inappropriately, resulting in waste and potential harm.

Employers need to understand this quickly emerging and complex area. The role that PGx tests play will greatly drive appropriate treatment decisions to help employers better manage pharmacy spend, which is especially critical as more biologics come to market.

### Definitions

Used interchangeably, [Personalized & Precision Medicine](#) focus on identifying which approaches will be most effective for which patients based on genetic, environmental, and lifestyle factors.

[Pharmacogenetics and Pharmacogenomics](#) are both part of precision medicine and also are used interchangeably, but each has its own distinction.

[Pharmacogenetics](#): Study how a person's genes affect the way they respond to drugs.

[Pharmacogenomics](#): Broader area of study on how the human genome may affect a person's response to drugs.

[Human Genome](#): Representation of all of the genetic or DNA information in a person. [The Human Genome Project](#) was founded in 1988 and led to the mapping of over 20,500 human genes in 2001.

[Genetic Testing](#): Sequencing of human DNA in order to discover genetic differences, anomalies, or mutations that may prove pathological.



For 11 years, MBGH's [National Employer Initiative on Specialty Drugs](#) has supported health benefits professionals in making critical and informed decisions to better manage specialty drug costs and offers guidance, tools and resources to support their efforts.

Check out the back page for more information and links to no-cost resources from this important employer-directed initiative.



*"It is key that employers understand this quickly developing area of pharmacy benefit management. This complex area of testing and the resulting data will become quite relevant as more and more biologics come to market and increase employer pharmacy spend. The role that these tests can play will help employers manage that spend."*

*Cheryl Larson, President & CEO, MBGH*

## How PGx Testing Works

From the way the drug enters our body to how the drug is broken down and gets to the intended area can be impacted by our DNA. There are four ways that DNA can impact how we respond to a drug. These are:

- 1) **Drug Receptors:** See Figure 1. Some drugs attach to proteins on the cells surface in order to be effective. DNA determines the number and type of receptors which impacts how we respond to the drug. Drug amounts and type differ amongst patients to achieve the desired result. Accurate prescribing of both the medication and dosage as well as how the drug is administered is essential here. Example: Breast Cancer and aligned therapies.
- 2) **Drug Uptake:** Some drugs need to enter into the tissues and cells. DNA impacts the uptake and removal of drugs from our cells. Blocked or decreased uptake can render the drug useless and can cause harmful drug build up in the body. If DNA causes the drug to be released from the cell too quickly, the drug may not have time to act. Example: Muscle Pain resulting from Statins.
- 3) **Drug Breakdown:** DNA can impact how quickly or slowly our body breaks down a drug. If too quickly, more drug may be required. If too slowly, less drug may be necessary. Adequate dosing is essential here for optimal treatment and disease management. Example: Depression and Amitriptyline.

- 4) **Targeted Drug Development:** PGx here is used to target the actual disease and not simply treat symptoms. Drugs and tests in this class target the gene mutations or changes. Drugs and tests here either seek to either correct the mutated protein or to replace it if missing. Example: Cystic Fibrosis and Ivacaftor.

For a deeper explanation and more information, please visit the [CDC Genomics website](#).

## PGx & Biologics

As evidenced by the complex mechanisms involved in drug interactions related to DNA, the connection to specialty drugs and in particular biologics and biosimilars, quickly comes into focus. [Biopharmaceuticals and biosimilars](#) are proteins and nucleic acids (DNA, RNA) not directly extracted using biotechnology. In order to be used by our bodies correctly, application of these drugs must consider our DNA and how drugs will be impacted.

While this area of testing within the pharmacy benefit is relatively new and remains to be designed and developed further, it is important to note that there is a need to define where the testing orders originate – the physician office or through the pharmacy benefit and the filling pharmacy. As more employer's demand access to PGx testing for biologics this issue will resolve itself.

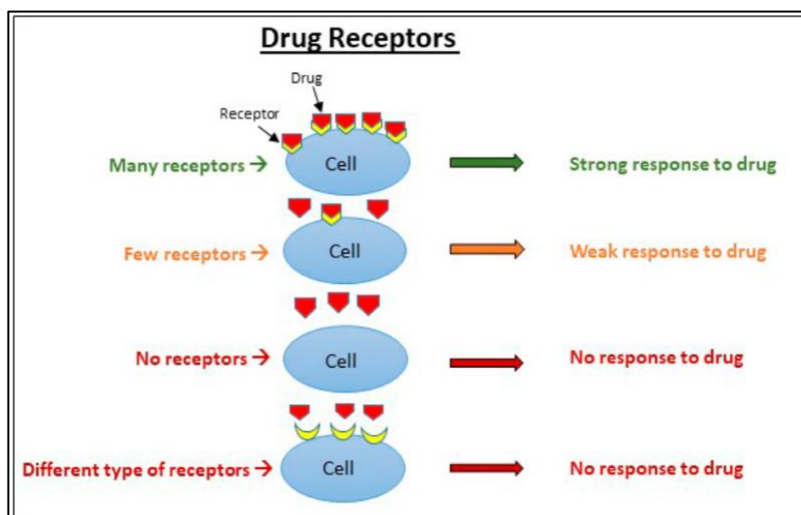


Figure 1: CDC on how PGx works using Drug Receptors

## The FDA and PGx

While the FDA does not typically oversee laboratory and other testing (normally left to the organization created out of the Clinical Laboratory Improvement Amendment of 1988 - CLIA) it does have oversight for PGx testing **as the tests are directly connected to access to a drug**. There has been a long-standing FDA position when it comes to genetic testing as a whole since the 1980s. (See these position papers specific to PGx testing: [October 3, 2014](#) and [October 31, 2018](#)) The actions from the FDA in recent years specific to PGx has been swift and thoughtful as they consider both the safety and the efficacy of these tests and their impact on the public.

The most recent rulings in 2020 by the FDA do show a softening of previous restrictions with a [more partnering approach](#) and providing a [public list of all PGx biomarkers in drug labeling](#) which is updated monthly. Companies offering PGx testing can now operate with clearer guidance and can develop tests to align with the approved biomarkers.

Employers should regularly be aware of the [FDA guidelines and regulations](#) related to PGx as they are evolving quickly.



## PGx testing barriers

While there are many reasons employers consider coverage of pre-emptive PGx testing as an employee health care benefit, there are also plan design considerations that must first be addressed, such as:

- selecting a testing vendor;
- determining which testing panels are most clinically useful for stratified groups of employees;
- deciding whether testing should be provided to all covered members or only those in risk groups;
- establishing payment methodologies, and
- ensuring this added benefit is legally compliant with HIPAA, GINA, EEOC, ADA and other regulations the biologic.

See next page for guidance on how to address above.

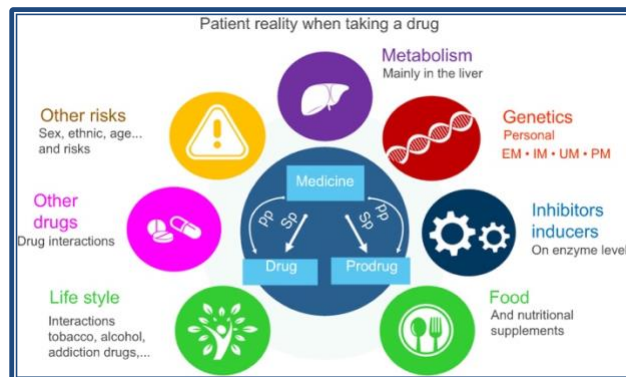
Physician reluctance and lack of knowledge to PGx is a common barrier. This can, in part, be attributed to physician unfamiliarity with PGx testing and the interpretation and application of results or the lack of awareness of local availability and reliability of testing resources. PGx remains unfamiliar territory to providers because it is new, with rapid growth in use of the testing over just the past decade—well after many practicing physicians and pharmacists graduated from degree programs and entered the field. Even physicians who received genetics education may feel unprepared to work with patients at high risk for genetic conditions and could lack confidence in interpreting PGx test results.

For employers, the lack of knowledge and initial understanding of the cost for PGx testing can also result in lower utilization. Further challenges employers will face relates to their current Pharmacy Benefit Manager (PBM) and their ability to interface with the selected testing vendor. Often times, the PBM is either not prepared for PGx claims or has already chosen a vendor of their own resulting in some employers carving out these services.





*"PGx testing is capable of bringing a new level of personalized medicine and cost containment to pharmacy benefit design and clinical management. The ability to precisely match a medication to a person's DNA allows for better disease control and medication therapy, offering savings for both the patient and company."*



## Employer Call to Action

Given that cost and quality care are top of mind for employers today, it is essential that adequate access and plan design features are in place to both ensure members have access and to control costs. Here are steps employers can take now:

### Action Steps for Employers

1. Learn more about precision medicine and PGx testing to enable discussions with employees, company leadership, health plan administrators and health care partners such as Carriers, TPAs and PBMs.
  - Participate regularly in meetings with your PBM's clinical pharmacists to both learn from them and to discuss how PGx can be effectively utilized within your plan.
  - Visit the [FDA website which lists all current PGx drugs and tests](#).
2. Select a PGx testing partner:
  - Run an RFP with relevant PGx testing providers to analyze and consider adding it to your plan as a carve out.
  - Discuss with your PBM any options they may have in place for PGx testing. Ensure you are not paying more for the tests than they are.
3. Lower barriers by assuring your health plan SPD states that evidence based PGx testing is a covered benefit and informing your medical carriers, PBMs and plan members about coverage. (See number 6)
4. Require use of PGx testing as part of prior authorization processes when [medications with FDA indicators](#) are prescribed for new use, in collaboration with the physician and a clinical pharmacist, if appropriate.
5. Educate plan members about opportunities PGx creates to match drugs to their personal genetic profile. Encourage them to ask their physicians if PGx testing is indicated when new medications are prescribed, or when medications being used are not producing desired treatment outcomes.
6. Incorporate clinical pharmacist enabled [Comprehensive Medication Management \(CMM\)](#) into your plan to facilitate use of PGx in precision medicine.
7. Eliminate misaligned financial incentives (rebates or other incentives) to approve one drug over another in the formulary. These incentives can distract efforts to leverage PGx effectively by placing matched drugs out of reach to members by access and/or cost.

*"PGx will bring a whole new meaning to pharmacy benefit management. To provide this testing will be essential."*



*"Most employers are challenged with implementing PGx as their PBM is not fully set up to deliver."*

## About this Report

The information provided in this report is based on the authors' and contributors' experiences working in the health benefits and health care industry. For more information on any aspect of the report, please contact [info@mbgh.org](mailto:info@mbgh.org).

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## New Pharmacy Benefit Services & No-Cost Resources for Employers

[Click on the links](#)

- [EmployeeRxEvolution \(ERxE\)](#) – Progressive employers are taking a bold step by integrating RxE into their pharmacy benefits fully transparent contract terms, custom formularies, direct contracts with retail pharmacies and evidenced-based PAs for specialty drugs.
- [Online Specialty Drug Employer Toolkit](#) - Offers no-cost tools, resources and checklists to support employer efforts, including:
- [Drawing a Line in the Sand: Employers Must Rethink Pharmacy Benefit Strategies](#)
- [Resolving to Control Drug Costs: Your PBM Contract Really Matters](#)
- [Designing Specialty Drug Benefits Checklist](#)
- [PBM Contract Checklist](#)
- [PBM Audit Recommendations](#)
- [Sites of Care Checklist](#)
- [Plan Member Education Strategy](#)

## New MBGH Employer Reports

MBGH recently released reports in the following areas to assist employers with their pharmacy benefit strategy.

1. [Biosimilars](#) – With more biosimilars coming to market this paper discusses this important drug category and how employers can be prepared.
2. [Authorized Generics](#) – Covers the availability and advantages of covering Authorized Generics (AG) in pharmacy benefit design. AGs offer a more costly and similar alternative to Brand drugs.
3. [Insulin Availability and Affordability](#) - This paper seeks to arm employers with key information about the insulin affordability and access problem facing many with the disease.

## The Power of MBGH!

Midwest Business Group on Health (MBGH) is one of the nation's largest non-profit coalitions of leading employers. Members are represented by human resources/health benefits professionals – collectively we serve as catalysts for change in addressing the US's health care challenges.



**130+ Members**  
Self-insured  
employers of all sizes



**\$12+ Billion**  
Employer members' annual  
health care benefits spend



**4 Million**  
Total lives  
represented